(12) UK Patent Application (19) GB (11) 2 166 354 A

(43) Application published 8 May 1986

(21) Application No 8523824

(22) Date of filing 27 Sep 1985

(30) Priority data

(31) 8425545 (32) 10 Oct 1984 (33) GB

(51) INT CL⁴
A61L 15/04

(52) Domestic classification
A5R BF

(56) Documents cited
None

(58) Field of search
A5R
A5B
C3R
Selected US specifications from IPC sub-class A61L

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(54) Wound dressings

(57) Wound dressings comprise a poly 3-hydroxybutyrate polymer dissolved or swollen with a volatile solvent such as chloroform. The 3-hydroxybutyrate may be co-polymerised with for example 10-30 mol % of 3-hydroxyvalerate units and may be in sterilised form e.g. by γ-radiation. On application to the wound the polymer adapts to the contours of the area to be treated and solvent evaporates to provide a film covering which is permeable to water vapour but impermeable to oxygen.

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SPECIFICATION

Wound dressings

The present invention relates to wound dressings and in particular to wound dressings comprising a polymer.

A variety of wound dressings is available for the treatment of wounds such as burns, cuts, abrasions and other skin disorders. In general gauze dressings are widely used; these have the disadvantage that they need to be changed frequently and application and removal can be painful for the wounded person. In addition gauze dressings may be inappropriate for certain conditions such as burns. Recently various polymeric materials have been proposed for wound care.

In Alvarez et al, Infections in Surgery 1984 p173, it is stated that three properties have been traditionally required for an optimal wound dressing. Firstly it should keep the wound surface moist and thus prevent crust formation. Secondly the wound temperature beneath the dressing should be as near to body temperature as possible to maintain optimal conditions for the functioning of enzymes. Thirdly the dressing should be oxygen permeable. However the article discloses that wounds covered with an oxygen impermeable hydrocolloid dressing healed at a greater rate than wounds covered with an oxygen permeable dressing. Dressings are known such as polyurethane films that are permeable to oxygen and to water vapour. In addition dressings are known, such as hydrocolloid films, that are impermeable to oxygen and water vapour. We have found that a dressing of poly 3-hydroxybutyrate (PHB) is particularly beneficial in the treatment of wounds, as it is permeable to water vapour but is oxygen impermeable. In addition such characteristics tend to prevent airborne bacterial contamination of the wound.

Poly(3-hydroxybutyrate) is a thermoplastic polyester consisting of repeat units of the formula $-CH(CH_3) . CH_2.CO.O-$ which is accumulated by many micro-organisms, particularly bacteria, for example of the genera Alcaligenes, Athiorhodium, Azotobacter, Bacillus, Nocardia, Pseudomonas, Rhizobium, and Spirillium, as an energy reserve material.

This material is non-toxic, compatible with living tissue without rejection or irritation and indeed the degradation product, 3-hydroxybutyric acid, is a normal mammalian metabolite. Poly-3-hydroxybutyrate is degraded over a period of time so that it is resorbed by the body without ill effects. In addition this material is hydrophilic so for use a wound dressing there is no need for an outer hydrophilic layer as is the case with many wound dressings. Thus a PHB dressing is considerably simpler than the multi-layer membranes of the art and does not need to be adhered to the skin with tape. In addition in some prior art treatments the wound site needs to be meticulously prepared, whereas the PHB dressing is, in one aspect, designed for rapid protection of a wound site with a temporary covering. Furthermore the PHB dressing is opalescent and, advantageously, enables viewing of the wound site without removal of the dressing.

Accordingly the present invention provides a wound dressing comprising poly 3-hydroxybutyrate dissolved or swollen with a volatile solvent.

In another aspect the present invention provides a poly 3-hydroxybutyrate dissolved or swollen with a volatile solvent for use as a wound dressing.

In a further aspect the present invention provides a method of treatment of a wound which comprises administering to a subject in need thereof an effective amount of poly 3-hydroxybutyrate dissolved or swollen with a volatile solvent.

The butyrate is applied to the wound as a solution or gel and adapts to the contours and creases of the area to be treated. Thus a thin film of polymer intimately contacts the treated area; this is of considerable benefit.

In general it is preferred that the film is formed rapidly as the dressing of this invention is of particular benefit for rapid and/or emergency treatment. In order that a film can be formed rapidly, the solvent preferably has a boiling point below 120°C, preferably below 80°C and preferably has a relatively high vapour pressure at ambient temperatures. With solvents having boiling points at the higher end of the range, it may be desirable to accelerate evaporation by applying a stream of air, preferably warmed, to the coating of the polymer/solvent composition on the wound area.

The butyrate polymer is soluble only in a restricted range of volatile solvents such as chlorinated hydrocarbons for example dichloromethane, chloroform and 1,2-dichloroethane. These then are preferred solvents and can be used alone or as mixtures thereof. In addition co-solvents may be added, in which the butyrate is not soluble, provided that precipitation does not occur. Such co-solvents include alcohols for example ethanol and propanol. Certain of these solvents are, of course, to be used with care to minimise the risk of inhalation of significant quantities by the subject being treated or the administrator of the dressing.

The composition preferably has a gel or syrupy consistency so that it can readily be applied to and spread over, the wound area without being so mobile that it would spread onto unwanted areas. The relative concentrations of polymer and solvent will depend on the nature of the solvent but will generally be such that the composition contains 2 to 15, preferably 5 to 12% by weight of the polymer.

Preferably the wound dressing of this invention is in sterilised form. Sterilisation can be performed on the butyrate prior to dissolution or gel formation, on the solution or gel in-situ. Any appropriate method may be used for example heating to the range 100-150°C or by γ-irradiation.

The butyrate polymer is conveniently prepared by cultivating the micro-organism in an aqueous medium on a suitable substrate, such as carbohydrate or methanol, as an energy and carbon source. The substrate must, of course, be one that is assimilable by the micro-organism. In order to promote accumulation of the polymer, at least part of the cultivation is preferably conducted under

conditions wherein there is a limitation of a nutrient that is essential for growth of the micro-organism but which is not required for polymer accumulation. Examples of suitable processes are described in EP-A-15669, 46344 and USP 4336334, 4433053.

Polymers containing both 3-hydroxybutyrate units and other hydroxycarboxylic acid units, such as 3-hydroxyvalerate units, can also be produced microbiologically. Thus a microbiologically produced heteropolymer containing 3-hydroxybutyrate and 3-hydroxyvalerate residues is described by Wallen et al in "Environmental Science and Technology" *8* (1974) 576-9. Also, as described in EP-A-52459, 69497 and USP 4477654 various copolymers can be produced by cultivating the micro-organism on certain substrates, such as propionic acid which gives rise to 3-hydroxyvalerate units in the copolymer.

The polymer can be extracted from the bacterial cells by a variety of techniques, often involving a solvent extraction step. Examples of such processes are described in EP-A-15123.

Accordingly, in the present specification, butyrate polymers cover the homo polymer, poly 3-hydroxybutyrate, and copolymers, obtained as described above, wherein the 3-hydroxybutyrate units form at least 40% mol%, and preferably at least 50 mol% of the polymer chain.

In a preferred aspect of this invention the butyrate is a copolymer consisting of 3-hydroxybutyrate and 3-hydroxyvalerate units, the amount of 3-hydroxyvalerate being in the range of about 10-30mol%. Such copolymers have improved flexibility compared to homopolymer films and have very good oxygen impermeability properties. This is thought by some authorities to be beneficial in promoting rapid healing of the wound. Preferably the amount of 3-hydroxyvalerate is about 20 mol%.

Copolymers tend to be soluble in a wider range of solvents and in some cases non-hazardous solvents such as propanol and higher alcohols can be employed although the compositions utilising such alcohols may tend to be gels rather than solutions.

In another aspect of the present invention the PHB wound dressing may comprise suitable medicinal agents for enhancing the healing of the wounds, for example antibiotics. The following Example serves to illustrate this invention:

A solution is made by dissolving 3-hydroxybutyrate/3-hydroxyvalerate copolymer containing about 17 mole % of 3-hydroxyvalerate units in chloroform. The solution has a syrupy consistency and contains 10% by weight of the copolymer. The solution could be sterilised by γ-irradiation.

When poured on to the back of a human hand the chloroform evaporates within a few minutes leaving a film of thickness about 10 um which adheres well to wounded and non-wounded parts of the skin and conforms to irregularities, e.g. creases, in the skin. The film is easily removed cleanly by peeling it off in large pieces.

CLAIMS

1. A wound dressing comprising a poly 3-hydroxybutyrate dissolved or swollen with a volatile solvent.
2. A wound dressing according to claim 1 wherein the poly 3-hydroxybutyrate comprises at least 50 mol% of 3-hydroxybutyrate units.
3. A wound dressing according to either claim 1 or claim 2 wherein the poly 3-hydroxybutyrate comprises 10-30 mol% of 3-hydroxyvalerate units.
4. A wound dressing according to claim 3 which comprises about 20 mol% of 3-hydroxyvalerate units.
5. A wound dressing according to any one of claims 1 to 4 in sterilised form.
6. A wound dressing according to any one of claims 1 to 5 wherein the solvent comprises chloroform.
7. A wound dressing comprising a poly 3-hydroxybutyrate.
8. A poly 3-hydroxybutyrate dissolved or swollen with a volatile solvent for use as a wound dressing as described in any one of claims 1 to 6.

Printed in the UK for HMSO, D8818935, 3/86, 7102.
Published by The Patent Office, 25 Southampton Buildings, London, WC2A 1AY, from which copies may be obtained.